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09/934,297	08/21/2001	Jennifer E. Van Eyk	PTQ-0037	8294
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LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			LAM, ANN Y	
ART UNIT	PAPER NUMBER	1641		

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/934,297	VAN EYK ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Ann Y. Lam	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 03 December 2004.  
 2a) This action is FINAL.                                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-8 and 29-56 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-8 and 29-56 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

## **DETAILED ACTION**

### ***Claim Objections***

Claim 52 is objected to because of the following informalities: “Igepal CA-360” should be –Igepal CA-360. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 and claim 50 recite “CHAPS”, which appears to be a trademark.

Claims 51 and 52 recite “Igepal CA-360”, “Triton X-100”, “Triton X-114”, “Tween”, “Tween 20” and/or “Tween 80”, which appear to be trademarks.

These trademarks are vague because the specification does not disclose their chemical formula, and chemical formulas of trademarks may change even though the trademark name may not change.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1, 2, 5, 8, 33-36, 41, 48, 51-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilotti et al., 5,994,507, in view of Schneider et al. 6,537,432, and further in view of Determann et al., 4,118,279.

Pilotti discloses the invention substantially as claimed. More specifically, Pilotti teaches a method of removing albumin from liquid samples for further processing of the liquid samples in the absence of albumin (column 1, lines 10-14).

However, Pilotti does not teach use of a reducing agent and detergents to denature albumin as a means to remove albumin from liquid samples for further processing of the liquid samples in the absence of albumin.

Schneider et al. teaches use of the claimed mixture of reagents. Schneider et al. teaches that typically protein samples to be separated are denatured (col. 11, lines 44-45), and nonionic detergents (e.g. igepal CA-360) or zwitterionic-surfactants can be used to suppress protein-wall and/or proteinprotein interactions that can result in protein precipitation (col. 11, lines 48-53). Schneider teaches that the denaturing buffer typically includes dithiothreitol to reduce any disulfide bonds present in the proteins. Schneider also teaches that other denaturants can be used (col. 11, lines 62-63).

Schneider discloses sodium dodecyl sulfate as one of the denaturants that may be additionally used (col. 28, line 45). Schneider also teaches the step of subjecting the mixture of biological sample and solution to a separation technique to separate proteins in the mixture (col. 30, line 54.)

Although Schneider et al. teaches that denaturants, such as dithiothreitol, will denature proteins in general, Schneider et al. does not specifically teach that the denaturant mixture actually denatures albumin. Determann et al. however teaches that dithiothreitol denatures albumin (col. 1, lines 36-38).

In sum, Pilotti teaches that it is desirable to remove albumin for further processing of a biological sample, and Schneider et al. teaches that proteins in a sample are typically denatured, using denaturants such as dithiothreitol, and the unwanted proteins removed from a biological sample for further processing of the sample. It would have been obvious to one of ordinary skill in the art at the time the invention was made that albumin can be removed in the Pilotti method by the denaturants taught by Schneider et al. because Schneider teaches that the denaturants denature and remove unwanted proteins from a sample for further processing of the sample, and Determan et al. teaches that the denaturants taught by Schneider et al., such as dithiotreitol, actually denatures albumin.

As to the remaining claims, Schneider et al. discloses the following.

As to claim 2, characterizing the separated proteins is disclosed (see Schneider et al., col. 31, lines 46-48).

As to claim 5, heating the mixture from step (a) prior to separation in step (b) is disclosed (see Schneider et al., col. 30, line 52).

As to claim 8, the anionic detergent is sodium dodecyl sulfate (see Schneider et al., col. 28, line 45).

As to claim 33, diluting said mixture of sample and solution prior to said separation step is disclosed (see Schneider et al., col. 30, lines 54-61.)

As to claim 34, said separation technique is affinity-based (see Schneider et al., col. 26, line 12).

As to claim 35, said separation technique comprises chromatography (see Schneider et al., col. 26 line 12).

As to claim 36, the chromatography is high performance liquid chromatography (HPLC), (see Schneider et al., col. 26, line 11.)

As to claim 41, the characterizing step comprises fluorescence detection (see Schneider et al., col. 3, line 67 – col. 4, line 1.)

As to claim 48, the references do not specifically teach that the sodium dodecyl sulfate is present in a concentration of from about 5 mM to about 150 mM. However, the range of concentration to achieve optimum results would require only routine experimentation and would thus be obvious. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

As to claims 51 and 52, the nonionic detergent is igepal CA-360 (see Schneider et al., col. 11, line 50.) (Since it appears that there is a spelling error in claim 52,

Examiner will assume for examination purposes that Applicant intends to means igepon CA-360, rather than ipegal CA-360.)

As to claim 53, the sulphydryl reducing agent is dithiothreitol (see Schneider et al., col. 11, lines 62-63.)

As to claim 54, the concentration of sulphydryl reducing agent that would achieve the optimum result would be discovered through routine experimentation. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

As to claim 55, said solution further comprises urea (see Schneider et al., col. 11, line 49).

As to claim 56, the concentration of urea that would achieve the optimum result would be discovered through routine experimentation. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

2. Claims 37, 38, 42 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilotti et al., 5,994,507, in view of Schneider et al., 6,537,432, further in view of Determann et al., 4,118,279, as applied to claim 1, and further in view of Figard, 5,616,460.

Pilotti et al. in view of Schneider et al., and further in view of Determann et al. discloses the invention substantially as claimed (see above with respect to claim 1.)

Schneider et al. teaches that the separated materials have further utility such as use in immuno-diagnostic assays (col. 27, lines 23-26.) However neither Schneider et al., nor Pilotti et al., nor Determann et al. teach the specific types of assays as claimed in claims 37, 38, 42 and 45.

Figard however teaches that these claimed types of assays are well known in the art for diagnosing the presence of an antigen for example.

More specifically, as to claim 37, Figard teaches contacting a protein in a mixture of proteins with an antibody (col. 1, lines 29-49).

As to claim 38, Figard teaches that the protein of the mixture is contacted with a first antibody, and said first antibody is contacted with a second antibody to the first antibody (col. 1, lines 42-49).

As to claim 42, Figard teaches that the characterizing step comprises colorimetric detection (col. 1, lines 48-49).

As to claim 45, Figard teaches that the characterizing step comprises detecting enzyme activity (col. 1, line 59-60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize these known types of assays and detection methods as disclosed by Figard after the step of separation of unwanted proteins in the method as taught by Pilotti et al., in view of Schneider et al., and further in view of Determann et al., because Figard teaches that these assay and detection methods provide the advantage of detecting and measuring the amount of antibody or antigen present (col. 1, lines 45-52.)

3. Claims 3, 4, 7, 29-32, 39, 40, 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilotti et al., 5,994,507, in view of Schneider et al. 6,537,432, further in view of Dermann et al., 4,118,279, and further in view of Schwartz et al., 6,020,139.

Pilotti et al., in view of Schneider et al., and further in view of Dermann et al. disclose the invention substantially as claimed (see above with respect to claims 1 and 2), except for the sample being serum, plasma, urine, amniotic fluid, cerebrospinal fluid, or the separation technique utilizing SDS-PAGE, or the characterizing step identifying a protein associated with myocardial or skeletal damage or comprises radiodetection or radiographic film.

Schwartz discloses these steps in diagnostic assays for the detection of diseases.

More specifically, as to claim 3, Schwartz discloses that the separation of proteins is by Western blot (column 63, line 19).

As to claim 4, Schwartz discloses that the sample comprises serum (column 12, line 9).

As to claim 7, the separation technique is performed using SDS-PAGE (column 63, line 17).

As to claim 29, the sample comprises plasma (column 12, line 9).

As to claim 30, the sample comprises urine (column 12, line 10).

As to claim 31, the sample comprises amniotic fluid (column 12, lines 10-11).

As to claim 32, the sample comprises cerebrospinal fluid (column 12, line 10).

As to claim 39, said characterizing step identifies at least one protein associated with myocardial damage (column 38, lines 6-9 and 43).

As to claim 40, said characterizing step identifies at least one protein associated with skeletal muscle damage (column 38, lines 6-9 and 43).

As to claims 43 and 44, said characterizing step comprises radiodetection and detection using radiographic film (column 5, line 33).

It would have been obvious to modify the method taught by Pilotti et al. in view of Schneider et al., and further in view of Determann et al. of preventing non-specific binding of albumin in assays, by using the particular assay taught by Schwartz because Schwartz teaches that these assays provide the advantage of detecting specific disease states and conditions such as myocardial damage.

4. Claims 6, 46 and 47, are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilotti et al., 5,994,507, in view of Schneider et al. 6,537,432, further in view of Determann et al., 4,118,279, and further in view of Rubenstein et al., 4,376,825.

Pilotti et al., in view of Schneider et al., and further in view of Determann et al. disclose the invention substantially as claimed (see above), except for the enzyme activity being horseradish peroxidase activity or alkaline phosphatase activity.

Rubenstein teaches these steps. More specifically, as to claim 6, the mixture is boiled (col. 57, line 29.)

As to claim 46, said enzyme activity is horseradish peroxidase activity (column 37, line 3). As to claim 47, said enzyme activity is alkaline phosphatase activity (column 50, line 45).

Rubenstein teaches that the disclosed method allows for determination of the amount of ligand present (col. 2, lines 65-68.) It would have been obvious that Rubenstein method of determining the amount of ligand present can be used in the method taught by Pilotti et al. in view of Schneider et al. in view of Dermann et al. of preventing non-specific binding of albumin in assays because Rubenstein et al. teaches that the disclosed enzymatic immunoassay provides the advantage of determining the amount of ligand present.

5. Claims 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilotti et al., 5,994,507, in view of Anderson et al., 5,993,627, and further in view of Dermann et al., 4,118,279.

Pilotti discloses the invention substantially as claimed. More specifically, Pilotti teaches a method of removing albumin from liquid samples for further processing of the liquid samples in the absence of albumin (column 1, lines 10-14).

However, Pilotti does not teach use of a reducing agent and detergents to denature albumin as a means to remove albumin from liquid samples for further processing of the liquid samples in the absence of albumin.

Anderson et al. discloses a method of separating a mixture of proteins in a biological sample (col. 6, lines 60-67) comprising:

(a) substantially denaturing protein in said sample (col. 6, line 48), wherein the sample is mixed with a solution comprising a sulphydryl reducing agent (i.e., dithiothreitol, col. 6, line 50.), and anionic detergent (i.e., sodium dodecyl sulfate, col. 4, line 11), and a non-ionic detergent (e.g., CHAPS, col. 6, line 49, and col. 16, lines 56-57),

and (b) subjecting the mixture of biological sample and solution to a separation technique to separate proteins in the mixture (col. 4, lines 15-19.)

As to claim 49, said zwitterionic detergent is CHAPS (col. 6, line 49 and col. 16, lines 56-57).

As to claim 50, the range of concentration of CHAPS that would achieve the optimum result would require only routine experimentation and would thus be obvious. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Although Anderson et al. teaches that denaturants, such as dithiothreitol, will denature proteins in general, Anderson et al. does not specifically teach that the

denaturant mixture actually denatures albumin. Determann et al. however teaches that dithiothreitol denatures albumin (col. 1, lines 36-38).

In sum, Pilotti teaches that it is desirable to remove albumin for further processing of a biological sample, and Anderson et al. teaches that proteins in a sample to be analyzed are typically first denatured, using denaturants such as dithiothreitol (see Anderson et al., col. 6, lines 47-50.) It would have been obvious to one of ordinary skill in the art at the time the invention was made that albumin can be removed in the Pilotti method by the denaturants taught by Anderson et al. because Anderson et al. teaches that the denaturants denature proteins prior to removal of unwanted proteins from a sample, and Determan et al. teaches that the denaturants taught by Anderson et al., such as dithiotreitol, actually denatures albumin.

### ***Response to Arguments***

Applicant's arguments with respect to the above rejected claims have been considered but are moot in view of the new ground(s) of rejection.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.L.



CHRISTOPHER L. CHIN  
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2/22/05